

**EXHIBIT C: MARKED VERSION OF CLAIMS**

U.S. APPLICATION SERIAL NO. To be assigned  
(ATTORNEY DOCKET NO. 9301-136)

(as amended April 2, 2001)

1. (Amended) A method for evaluating specificity of a drug comprising comparing activity of said drug against its target pathway ( $D_{target}$ ) in a biological sample and activity of said drug against at least one off-target pathway ( $D_{off-target}$ ) in said biological sample, wherein said  $D_{target}$  and  $D_{off-target}$  are based on measurements of a plurality of cellular constituents.

12. (Amended) A method for evaluating specificity of a drug comprising:

- a) measuring activity of said drug against its target pathway to obtain a target activity ( $D_{target}$ );
- b) measuring activity of said drug against at least one pathway other than said target pathway to obtain at least one off-target activity ( $D_{off-target}$ ); and
- c) determining said specificity by comparing said target activity and said off-target activity;

wherein said  $D_{target}$  and  $D_{off-target}$  are based on measurements of a plurality of cellular constituents.

23. (Amended) A method of determining therapeutic index of a drug in a biological sample comprising:

determining said therapeutic index according to the formula: [SI]  $TI = C_{target} / C_{off-target}$ , wherein  $C_{target}$  is a minimum effective concentration needed to induce a threshold response in a target pathway and  $C_{off-target}$  is the minimum toxic concentration needed to induce a threshold response in at least one off-target pathway.

24. (Amended) The method of claim 23 wherein said  $C_{target}$  and  $C_{off-target}$  are measured according to a method comprising:

- a) applying a plurality of levels of said drug to said biological sample and measuring a plurality of cellular constituents at each level of said drug in said biological sample to obtain a first profile of graded drug response;

b) applying said plurality of levels of said drug to a test sample, wherein said test sample is the same as said biological sample except that said target pathway is not functional, and measuring a plurality of cellular [constituents] constituents in said test sample at each level of said drug, to obtain a second profile of graded drug response; and

c) determining said  $C_{target}$  and  $C_{off-target}$  by comparing said first and second profiles.

34. (Amended) A method of determining a therapeutic index of a drug in a biological sample comprising:

a) applying a plurality of levels of said drug to said biological sample;

b) determining a minimum effective concentration ( $C_{target}$ ) needed to induce a threshold response in a target pathway, wherein said drug exerts its pharmacological activity through said target pathway;

c) determining a minimum toxic concentration ( $C_{off-target}$ ) needed to induce a threshold response in at least one off-target pathway; and

d) determining said therapeutic index according to the formula: [SI] TI =  $C_{target} / C_{off-target}$ .

36. (Amended) The method of claim 35 [herein] wherein said plurality of cellular constituents are transcripts of a plurality of genes.

New claims 64-70 have been added.

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